

## Technology Offer

### Combined PI3-Kinase- and SUMO inhibitor therapy for Pancreatic Cancer

Ref. No.: CH181

#### Background

Pancreatic ductal adenocarcinoma (PDAC) is one of the most aggressive and deadliest cancers, with a 5-year survival rate of just 13%. Despite its increasing incidence, also in younger patients, treatment options for PDAC remain limited and non-satisfying. *KRAS* mutations (in 90% of cases) position the *KRAS*/MAPK signaling pathway as a central driver of tumor progression and a critical therapeutic target. Recently developed RAS inhibitors, have shown promising early signs of clinical efficacy in PDAC. However, genetic and adaptive resistance to RAS inhibition remains challenging. Isoform-specific Phosphatidylinositol-3-Kinase (PI3K) inhibitors have been tested in clinical trials for solid tumors, including PDAC, however they exhibited limited efficacy. Targeting the small ubiquitin-like modifier (SUMO)ylation pathway has shown efficacy in PDAC and other malignancies in preclinical models. Despite the advancements, there is still an unmet need to provide additional effective treatment strategies in PDAC, that inhibits tumor progression and improves clinical outcomes.

#### Technology

Based on new findings that the PI3K-pathway and the SUMO-pathway interact with each other in the way that blockage of the PI3K-pathway activates the SUMO-pathway and vice versa, a novel therapeutic approach for treating PDAC has been developed by combining a PI3-K  $\alpha/\delta$  inhibitor with a SUMO-inhibitor. In patient derived pancreatic organoids from mesenchymal/basal-like PDAC patients, the combination of Pictilisib (PI3-K  $\alpha/\delta$ -inhibitor) and Subasumstat increases cell death more strongly than Pictilisib or Subasumstat alone. In an immune-competent mice model in which syngeneic orthotopic tumor grafts were generated, the combined inhibition of PI3-K  $\alpha/\delta$  by Copanlisib and SUMO by Subasumstat reduced tumor growth significantly compared to untreated mice. Inhibiting both pathways leads to an unexpected synergistic effect: Monotherapy with Subasumstat or Copanlisib alone is less effective and not significant compared to untreated mice. Therefore, the new combination of an PI3-K  $\alpha/\delta$  inhibitor with a SUMO-inhibitor is a new promising treatment strategy to inhibit tumor progression in PDAC.

#### Benefits

- ✓ Synergistic anti-tumor effect by using PI3-K  $\alpha/\delta$ - and SUMO-inhibitor
- ✓ Quantitative synergy evident in in vitro, ex vivo and in vivo settings and also for various combinations

#### Application

Dual combination inhibitor therapy in pancreatic cancer

#### Commercial Opportunity

Searching for a licensing and/or developing partner

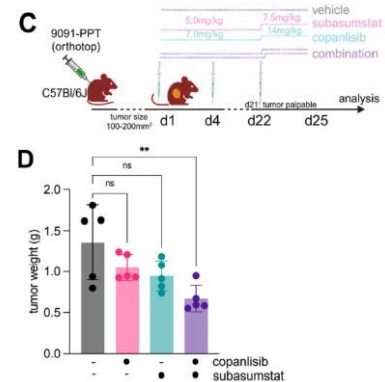


Fig. 1: In an immune-competent mice model in which syngeneic orthotopic tumor grafts were generated, the combined PI3K $\alpha/\delta$  inhibitor-SUMO-inhibitor treatment significantly reduces the tumor growth compared to untreated mice.

#### Key words

Pancreatic ductal adenocarcinoma, PI3-Kinase inhibitor, SUMO-inhibitor, tumor, dual combination therapy, sumoylation, Copanlisib, Subasumstat

#### Developmental Status

*In vivo* (mice efficacy data), *ex vivo* (human organoids), *in vitro*

#### IP Status

EP priority patent application: EP 25189303.8, filed 07/2025

#### Patent Owner

Charité – Universitätsmedizin Berlin  
Georg-August-Universität Göttingen

#### Further Reading

Köse and Wirth et al. 2025;  
[Gastroenterology 2025;1-15](#)

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